

REPORT DOCUMENTATION PAGE

Form Approved
OMB NO. 0704-0188

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1. AGENCY USE ONLY (Leave Blank)		2. REPORT DATE 04/14/00		3. REPORT TYPE AND DATES COVERED Final	
4. TITLE AND SUBTITLE 1999 Gordon Research Conference on Lipid Metabolism				5. FUNDING NUMBERS DAAD19-99-1-0151	
6. AUTHOR(S) Prof. William Dowhan, PI					
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Gordon Research Conferences PO Box 982 West Kingston, RI 02892-0984				8. PERFORMING ORGANIZATION REPORT NUMBER 1 of 1	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U. S. Army Research Office P.O. Box 12211 Research Triangle Park, NC 27709-2211				10. SPONSORING / MONITORING AGENCY REPORT NUMBER ARO 39775.1-LS-CF	
11. SUPPLEMENTARY NOTES The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision, unless so designated by other documentation.					
12 a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited.				12 b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 words) The 1999 Gordon Research Conference on Molecular and Cellular Biology of Lipids was held June 27 – July 2 at Kimball Union Academy in Meriden, NH. The attendees represented a broad group of participants. Each session brought out new and important information in the following fields: Biochemistry and Genetics of Lipid A; Lipid Movement and Translocation; Vesicle Trafficking and Lipid Transfer Proteins; Lipids as Signaling Molecules; Genetics and Biochemistry of Sterol Metabolism; Genetics and Biochemistry of Lipid Metabolism in Somatic Cells; Lipid Metabolism in Microbial Systems; Phospholipid-Lipid Interactions; and Fatty Acid and Triacylglycerol Metabolism.					
14. SUBJECT TERMS Lipid Metabolism				15. NUMBER OF PAGES 15	
				16. PRICE CODE	
17. SECURITY CLASSIFICATION OR REPORT UNCLASSIFIED	18. SECURITY CLASSIFICATION ON THIS PAGE UNCLASSIFIED	19. SECURITY CLASSIFICATION OF ABSTRACT UNCLASSIFIED	20. LIMITATION OF ABSTRACT UL		

Conference Chair's Report

The 1999 Gordon Research Conference on Molecular and Cellular Biology of Lipids was held June 27-July 2 at Kimball Union Academy in Meriden, NH. This conference is held in odd numbered years and was last held in 1997. As has been typical of this meeting except for the 1997 meeting, it was oversubscribed and only 140 of the 158 applicants could be accommodated. There were 18 graduate students, 19 postdoctoral fellows: the remainder were more senior scientists that included principle investigators and senior research scientists. There were initially 30 invited speakers who gave full talks (30-35 minutes). Of this group 2 were graduate students. The attendees represented a broad list of participants as summarized in the attached information. This year 8 additional speakers were selected based on abstracts describing work that was submitted to be presented in poster form. These speakers were allotted 15 minutes to summarize and highlight their findings that were expanded on in the poster sessions. Five of these 8 speakers were graduate students. Of the total of 38 speakers, 9 were women, 20 had not spoken previously at this Gordon Conference, and only 3 had spoken at the previous conference (1997). The full-length talks were followed by 10-15 minutes of discussion time and the short talks were followed by 5 minutes of discussion time. The discussion time was fully utilized in all cases indicating significant involvement by all attendees. Every attendee was strongly encouraged to present a poster in one of the 2 poster sessions held during the 4 full days of the conference. During this period there were 84 posters presented.

Each session brought out new and important information in the respective fields as summarized below.

Biochemistry and Genetics of Lipid A

1. First presentation of the organization of Lipid A molecular bound to a protein.

This is also the only information we have of how the three-dimensional structure of Lipid A.

2. Identification and activation of a set of genes in *E. coli* that result in modification of Lipid A to resemble more closely Lipid A found in pathogenic organisms. These normally silent genes may be related to the pathogenesis in other organisms.

Lipid Movement and Translocation

1. More detailed understanding of the components of the phospholipid transport machinery. In particular the genetic separation of lipid movement between organelles from lipid fusion with organelles.
2. The exciting finding that translocation of phospholipids across the cytoplasmic membrane of somatic cells is essential for cell division.
3. A summary of plasma membrane phospholipid transbilayer movement indicating that the proteins and processes studied over the past few years may not be representative of the true biological process.
4. A new mode of regulation of phospholipid transbilayer movement that appears to be regulation through protein phosphorylation.

Vesicle Trafficking and Lipid Transfer Proteins

1. Description of additional somatic-cell homologues of the yeast Sec14p phospholipid transfer proteins. Transfection studies pointing to their physiological function.
2. Conclusive evidence for the participation of lipid rafts in organization a subset of transport vesicles that bud from the Golgi for the specific transport of GPI-anchored proteins.
3. Further evidence of the involvement of phosphorylated phospholipid intermediates in secretion and endocytosis.
4. This whole session provided compelling evidence of the active rather than passive role of membrane lipids in biological processes.

Lipids as Signaling Molecules

1. Further documentation that recently discovered diacylglycerol pyrophosphate is a lipid second messenger.
2. New evidence indicating that in yeast phosphorylated long-chain base precursors to ceramide and not ceramide itself are second messengers.
3. A delineation of the complex mixture of diacylglycerol kinases isozymes with presentation of evidence for specific kinases involved in compartmentalized and specific processes.

Genetics and Biochemistry of Sterol Metabolism

1. Evidence that 3 oxysterols that lie along the biosynthetic pathway to bile acids are important regulators of cholesterol biosynthesis.
2. Impressive crystal structures of farnesyl transferase in association with its lipid substrate. These structures revealed important mechanistic information and information necessary for specific drug design.
3. A complete description of the evolving understanding of the regulation of cholesterol biosynthesis via the endoplasmic membrane proteases that activate nuclear transcription factors.
4. Similar coordinate regulation of phosphatidylcholine biosynthesis in response to the release of transcription factors regulating cholesterol biosynthesis.

Genetics and Biochemistry of Lipid Metabolism in Somatic Cells

1. Evidence supporting a role for phosphatidylethanolamine methylase in liver during periods of choline starvation.
2. Description of mutants in somatic cell sphingomyelin biosynthesis that will be very useful in determining the role of this lipid in cell function.
3. Description of a new CTP:phosphocholine cytidyltransferase encoded by a second gene. The tissue and intracellular distribution of this gene product differs from the previously described isozyme.

Lipid Metabolism in Microbial Systems

1. Evidence that an early intermediate (possibly phosphatidic acid) and not phosphatidylcholine is the regulator of aminophospholipid metabolism in yeast.
2. Documentation that cardiolipin is not essential in yeast and that the primary defects observed in mitochondrial function in mutants lacking cardiolipin appears to be more closely associated when phosphatidylglycerol is also limiting.
3. The first report of a CDP-diacylglycerol-dependent phosphatidyl transferease utilized to synthesize phosphatidylcholine was made. This *Pseudomonas* enzyme may be wide spread among bacteria that have a symbiotic relationship with a somatic cell host.
4. A crystal structure of a bacterial cytidyltransferase was presented that advanced our understanding of the mechanism of related somatic cell enzymes.

Phospholipid-Lipid Interactions

1. Bacterial leader peptidase has a hydrophobic patch that allows its active site to penetrate the membrane to gain access to the hydrophobic domain of its

substrate much like the protease that acts to release cholesterol biosynthetic regulators.

2. A clear relationship between the initiation of DNA replication in bacteria and association of initiation complex with the membrane through anionic lipids was demonstrated.
3. Extensive evidence was presented in 2 talks that establish lipids (phospholipids and precursors to lipopolysaccharides) as true molecular chaperones in the assembly of membrane proteins.
4. Extension of the use of lipid cubic phase for the crystallization of membrane proteins was presented.

Fatty Acid and Triacylglycerol Metabolism

1. A new role for Acyl-CoA in the regulation of all of intermediate metabolism in the pancreas was presented
2. Crystal structure of 2 important enzymes in bacterial fatty acid biosynthesis was presented. Molecular modeling revealed substrate binding sites and sufficient new information for the design of drugs.
3. The phenotype and properties were presented for the first time of a knock-out mouse with a defect in diacylglycerol acyltransferase. The results will require a re-evaluation of our understanding of triacylglycerol metabolism.

The poster sessions were well-attended and active discussions continued during the whole allotted time. Many of the speakers referred to and integrated the posters into their presentation. The presentation of 8 talks from the poster submissions helped to integrate these two aspects of the meeting. Overall the conference had a broad participation from outside the core of regular attendees, from young and established investigators, and by women scientists. The participation of graduate students in the speaking program was a great success and helped to stimulate discussion and the presentation of current results. The comments received by participants during the meeting indicated that the meeting was very successful. Those who have attended regularly comment on the high quality of the science presented and the level of enthusiastic participation. New comers to this conference were very impressed with all aspects of the conference in comparison to other Gordon Conferences attended. First-time Gordon participants were overwhelmingly positive about their experience and were already anticipating future meetings. The session chairs and past conference chairs were very positive about the overall conference format and were very positive about the addition of the short talks from the poster sessions.

Molecular & Cellular Biology of Lipids

Kimball Union Academy
Meriden, New Hampshire, USA
June 27-July 2, 1999

Chair: **William Dowhan**
Vice Chair: **Charles Rock**

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- **7:30** Site Director's Remarks
 - **7:45** ***William Dowhan**. University of Texas Medical School, Houston, TX
Welcome and Introductions
 - **8:00** **Christian R. H. Raetz** Duke University Medical Center, Durham, NC
Keynote Address: Assembly and Function of Gram-Negative Endotoxin: From Genomics to Structural Biology (Alexander M. Cruickshank Lecturer)
 - **9:00** **Eckhard Hofmann** University of Konstanz, Konstanz, Germany
The X-ray structure of Gram-Negative endotoxin and its interaction with the outer membrane protein FhuA
 - **9:45** Welcome Reception
-

- **8:30 *Dennis R. Voelker.** National Jewish Center, Denver, CO
Biochemical and Genetic Analysis of Intracellular Phospholipid Movement
- **9:15 Masato Umeda.** Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan
Regulation of Cell Division by Transbilayer Relocation of Membrane Phospholipids
- **10:00** Coffee Break
- **10:20 Peter J. Sims.** Scripps Research Institute, La Jolla, CA
Structure and Function of Plasma Membrane Phospholipid Scramblase: A Protein Mediating Ca²⁺ Initiated Cell Surface Exposure of Aminophospholipids
- **11:05 Jerome F. Strauss.** University of Pennsylvania, Philadelphia, PA
Regulation and Function of STAR, a Sterol Transfer Protein
- **11:50 S. Courtney Frasch.** National Jewish Center, Denver, CO
Regulation of Phospholipid Scramblase Activity during Apoptosis by PKC δ

Poster Chair, **Charles Rock**

- **7:30 *Vytas A. Bankaitis.** University of Alabama, Birmingham, AL
Role of Phospholipid Transfer Proteins in Cell Function
- **8:15 Howard Riezman.** University of Basel, Basel, Switzerland
Role of Ongoing Ceramide Synthesis in ER to Golgi Transport of GPI-Anchored Proteins
- **9:00 Andy Wurmser.** University of California-San Diego, La Jolla, CA
3'-Phosphoinositide Regulation of Secretory and Endocytic Trafficking Pathways
- **9:45 Kristin B. Hendricks.** University of California, Berkeley, Berkeley, CA
*Yeast Homolog (*Frq1*) of Neuronal Frequentin is a Positive Regulator of Phosphatidylinositol 4 Kinase*

- **8:15 *George M. Carman.** Rutgers University, New Brunswick, NJ
Molecular Characterization and Regulation of Lipid Phosphate Phosphatases
- **9:00 Robert C. Dickson.** University of Kentucky College of Medicine, Lexington, KY
*Roles for Sphingolipids in *Saccharomyces* Heat and Nutrient Stress Responses*
- **9:45** Coffee Break
- **10:05 Yusuf A. Hannun.** Medical University of S. Carolina, Charleston, SC
Sphingolipid Metabolism and the Eukaryotic Stress Response
- **10:50 Stephen M. Prescott.** University of Utah, Salt Lake City, Utah
Regulation of cellular responses by diacylglycerol kinases
- **11:35 Vicki A. Sciorra.** Stony Brook Health Sciences Center, Stony Brook, NY
Identification of a Phosphoinositide Binding Motif that Mediates Activation of Yeast and Mammalian Phospholipase D Isoenzymes
- **12:00** Meeting Picture

Poster Chair, Charles Rock

- **7:30 *David Russell.** University of Texas Southwestern Medical Center, Dallas, TX
Oxysterols: Regulators and Breakdown Products of Cholesterol Metabolism
- **8:15 Lorena S. Beese.** Duke University Medical Center, Durham, NC
Structure and mechanism of protein farnesyl transferase
- **9:00 Michael S. Brown.** University of Texas Southwestern Medical Center, Dallas, TX
Regulation of Cholesterol Metabolism
- **9:45 Neale D. Ridgway.** Dalhousie University, Halifax, Nova Scotia, Canada
Regulation of Phosphatidylcholine Synthesis by the Sterol Regulatory Element Binding Protein (SREBP) / SREBP Cleavage Activating Protein (SCAP) Pathway

- **8:30 *Dennis Vance.** University of Alberta, Alberta, Canada
Role of PE Methylation in Hepatic Function and Transcriptional Regulation of CTP:Phosphocholine Cytidyltransferase
- **9:15 Masahiro Nishijima.** National Institutes of Infectious Disease, Tokyo, Japan
Sphingomyelin biosynthesis: Studies in CHO mutants resistant to a SM-directed cytolysin
- **10:00** Coffee Break
- **10:20 Salih Wakil.** Baylor College of Medicine, Houston, TX
Structure and Mechanism of Fatty Acid Synthase
- **11:05 Martin Post.** Hospital for Sick Children, Toronto, Canada
Molecular regulation of CTP:Phosphocholine Cytidyltransferase in the developing lung
- **11:50 Athanasios Lykides.** St. Jude Children's Research Hospital, Memphis, TN
CTP:Phosphocholine Cytidyltransferase Isoforms: Their Tissue Distribution and Subcellular Localization

Poster Chair, Charles Rock

- **7:30 *Susan Henry.** Carnegie Mellon University, Pittsburgh, PA
Regulation of Phospholipid Metabolism in Yeast
- **8:15 Miriam Greenberg.** Wayne State University, Detroit, MI
Cardiolipin Biosynthesis and Function in Yeast
- **9:00 Otto Geiger.** Technical University of Berlin, Berlin, Germany
Novel Phosphatidyltransferases Involved in Phosphatidylcholine Biosynthesis
- **9:45 Claudia Kent.** University of Michigan, Ann Arbor, MI
Structure and Substrate Affinities of Glycerol-3-Phosphate Cytidyltransferase

-
- **8:30 *Ben de Kruijff.** Utrecht University, Utrecht, The Netherlands
The Bilayer Paradox of Membranes
 - **9:15 Elliott Crooke.** Georgetown University Medical Center, Washington, D. C.
Role of Anionic Phospholipids in the Initiation of DNA Replication
 - **10:00** Coffee Break
 - **10:20 Mikhail Bogdanov.** University of Texas Medical School, Houston, TX
Phospholipid-Assisted Folding and Topological Assembly of Membrane Proteins
 - **11:05 Ehud Landau.** University of Basel, Basel, Switzerland
Crystallization in "cubo": General applicability to membrane proteins
 - **11:50 Hans de Cock.** University of Utrecht, Utrecht, The Netherlands
Lipopolysaccharide- and Phospholipid-Dependent Folding of Outer Membrane Proteins
-

Poster Chair, **Charles Rock**

- **7:30 *Rosalind A. Coleman.** University of North Carolina, Chapel Hill, NC
Mitochondrial Glycerophosphate Acyltransferase: Regulation of Acyl-CoA Partitioning
 - **8:15 Barbara Corkey.** Boston University Medical Center, Boston, MA
Physiological Role for Acyl-CoA in Regulation of Insulin Secretion
 - **9:00 Charles O. Rock.** St. Jude Children's Research Hospital, Memphis, TN
High-Resolution Structure and Mechanism of Type II Fatty Acid Synthesis
 - **9:45 Steve J. Smith.** Gladstone Institute of Cardiovascular Disease, San Francisco, CA
DGAT Knockout Mice: Obesity Resistance and Evidence for an Alternative Triacylglycerol Synthesis Pathway
-

* Denotes Session Chairs/Discussion Leaders



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LIPIDS, MOLECULAR & CELLULAR BIOLOGY OF

Kimball Union Academy, Meriden, NH
(27-Jun-99) - (02-Jul-99)

This was the final registration list for the 1999 Conference on
LIPIDS, MOLECULAR & CELLULAR BIOLOGY OF.

<u>SREENIVAS AVULA</u>	RUTGERS UNIVERSITY	Poster Presenter	Accepted
<u>MARICA BAKOVIC</u>	UNIVERSITY OF ALBERTA	Poster Presenter	Registered
<u>BENEDICTE C BALCERZAK</u>	UNIVERSITY OF ALBERTA	Poster Presenter	Registered
<u>VYTAS A BANKAITIS</u>	UNIVERSITY OF ALABAMA AT BIRMINGHAM	Speaker	Registered
<u>SUZANNE E BARBOUR</u>	VIRGINIA COMMONWEALTH UNIVERSITY	Poster Presenter	Registered
<u>LORENA S BEESE</u>	DUKE UNIVERSITY MEDICAL SCHOOL	Speaker	Registered
<u>CHRISTOPH BENNING</u>	MICHIGAN STATE UNIVERSITY	Attendee	Registered
<u>PAUL N BLACK</u>	ALBANY MEDICAL COLLEGE	Poster Presenter	Registered
<u>MIKHAIL BOGDANOV</u>	UNIV OF TEXAS MED SCHOOL AT HOUSTON	Speaker	Registered
<u>CLAUS BORSTING</u>	ALBANY MEDICAL COLLEGE	Poster Presenter	Registered
<u>DAWN L BRASAEMLE</u>	MCP HAHNEMANN UNIVERSITY	Poster Presenter	Registered
<u>DONNA BRATTON</u>	NATIONAL JEWISH HOSPITAL	Poster Presenter	Registered
<u>DAVID N BRINDLEY</u>	UNIVERSITY OF ALBERTA	Poster Presenter	Registered
<u>ANGELEAH BROWDY</u>	UNIVERSITY OF RHODE ISLAND	Poster Presenter	Registered
<u>MICHAEL S BROWN</u>	UNIVERSITY OF TEXAS SOUTHWESTERN MEDICAL CENTER	Speaker	Registered
<u>STUART BURSTEN</u>	CELL THERAPEUTICS, INC.	Attendee	Registered
<u>MYLES C CABOT</u>	JOHN WAYNE CANCER INSTITUTE	Attendee	Registered
<u>GEORGE M CARMAN</u>	RUTGERS UNIVERSITY	Speaker	Registered
<u>JEAN CHIN</u>	NIH-NIGMS-CBB	Attendee	Registered
<u>CATHERINE F CLARKE</u>	UNIVERSITY OF CALIFORNIA, LOS ANGELES	Poster Presenter	Registered
<u>ROSALIND A COLEMAN</u>	UNIVERSITY OF NORTH CAROLINA	Speaker	Registered
<u>ISABELLE COPPENS</u>	YALE UNIVERSITY	Attendee	Registered
<u>BARBARA E CORKEY</u>	BOSTON UNIVERSITY MEDICAL CENTER	Speaker	Registered
<u>ROSEMARY B CORNELL</u>	SIMON FRASER UNIVERSITY	Attendee	Registered
<u>BETINA CORSICO</u>	INIBIOLP	Poster Presenter	Registered
<u>AIDA E CREMESTI</u>	UNIVERSITY OF RHODE ISLAND	Poster Presenter	Registered
<u>ELLIOTT CROOKE</u>	GEORGETOWN UNIVERSITY MEDICAL CENTER	Speaker	Registered
<u>ZHENG CUI</u>	WAKE FOREST UNIVERSITY SCHOOL OF MEDICINE	Attendee	Registered
<u>ALAN W CURNOW</u>	PROCTER & GAMBLE PHARMACEUTICALS	Attendee	Registered
<u>HANS DE COCK</u>	UTRECHT UNIVERSITY	Poster Presenter	Registered
<u>ANTON I.P.M. DE KROON</u>	UTRECHT UNIVERSITY	Poster Presenter	Registered
<u>BEN DE KRUIJFF</u>	UTRECHT UNIVERSITY	Discussion Leader	Registered
<u>NIHAL S DESILVA</u>	SOUTHERN BIOGENE LAB	Discussion Leader	Accepted
<u>DARYLL B DEWALD</u>	UTAH STATE UNIVERSITY	Poster Presenter	Registered
<u>ROBERT C DICKSON</u>	UNIVERSITY OF KENTUCKY COLLEGE OF MEDICINE	Speaker	Registered
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<u>MICHEL LAGARDE</u>	INSA/INSERM	Poster Presenter	Accepted
<u>EHUD LANDAU</u>	UNIVERSITY OF BASEL	Speaker	Registered
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<u>CONSTANTINE LONDOS</u>	NIDDK, NIH	Attendee	Registered
<u>ATHANASIOS LYKIDIS</u>	ST JUDE CHILDREN HOSPITAL	Poster Presenter	Registered
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<u>MARKKU J SAVOLAINEN</u>	UNIVERSITY OF OULU	Attendee	Registered
<u>HARALD H SCHMID</u>	UNIVERSITY OF MINNESOTA	Poster Presenter	Registered
<u>BARBARA M SCHREIBER</u>	BOSTON UNIV. SCHOOL OF MEDICINE	Poster Presenter	Registered

<u>VICKI A SCIORRA</u>	SUNY AT STONY BROOK	Poster Presenter	Registered
<u>PETER J SIMS</u>	THE SCRIPPS RESEARCH INSTITUTE	Speaker	Registered
<u>SING-YUEN SIT</u>	BRISTOL-MEYERS SQUIBB COMPANY	Attendee	Registered
<u>MAREK S SKRZYPEK</u>	UNIVERSITY OF KENTUCKY MEDICAL CTR	Attendee	Registered
<u>J. DONALD SMITH</u>	UNIVERSITY OF MASSACHUSETTS, DARTMOUTH	Attendee	Registered
<u>STEVE SMITH</u>	GLADSTONE INSTITUTE CARDIOVASCULAR DISEASE	Poster Presenter	Registered
<u>FRIEDRICH SPENER</u>	UNIVERSITY OF MUENSTER	Speaker	Registered
<u>VICTORIA L STEVENS</u>	EMORY UNIVERSITY SCHOOL OF MEDICINE	Poster Presenter	Registered
<u>JUDY STORCH</u>	RUTGERS UNIVERSITY	Poster Presenter	Registered
<u>JEROME F STRAUSS</u>	UNIVERSITY OF PENNSYLVANIA	Speaker	Registered
<u>XUEFENG SU</u>	UNIVERSITY OF TEXAS-HOUSTON	Poster Presenter	Registered
<u>CELESTINE J THOMAS</u>	MOLECULAR BIOPHYSICS UNIT	Poster Presenter	Accepted
<u>ALFRED E THUMSER</u>	RUTGERS UNIVERSITY	Poster Presenter	Registered
<u>KHAI T TRAN</u>	UNIVERSITY OF OTTAWA HEART INSTITUTE	Poster Presenter	Registered
<u>MICHAEL S TRENT</u>	DUKE UNIVERSITY MEDICAL CENTER	Poster Presenter	Registered
<u>PAMELA J TROTTER</u>	UNIVERSITY OF TEXAS AT AUSTIN	Poster Presenter	Registered
<u>MASATO UMEDA</u>	TOKYO METROPOLITAN INSTITUTE OF MEDICAL SCIENCE	Speaker	Registered
<u>ARIE B VAANDRAGER</u>	UNIVERSITY OF UTRECHT	Attendee	Registered
<u>JEAN E VANCE</u>	UNIVERSITY OF ALBERTA	Poster Presenter	Registered
<u>DENNIS E VANCE</u>	UNIVERSITY OF ALBERTA	Speaker	Registered
<u>DENNIS R VOELKER</u>	NATIONAL JEWISH CENTER	Speaker	Registered
<u>SALIH WAKIL</u>	BAYLOR COLLEGE OF MEDICINE	Speaker	Registered
<u>PAUL A WEINHOLD</u>	UNIV OF MICHIGAN & VA MEDICAL CENTER	Poster Presenter	Registered
<u>THERESE WIEDMER</u>	THE SCRIPPS RESEARCH INSTITUTE	Attendee	Registered
<u>WEN-I WU</u>	NATIONAL JEWISH MEDICAL & RESEARCH CENTER	Poster Presenter	Registered
<u>ANDREW WURMSER</u>	HOWARD HUGHES MEDICAL INSTITUTE	Speaker	Registered
<u>XIAORUI YAO</u>	SCHERING-PLOUGH RESEARCH INSTITUTE	Poster Presenter	Registered
<u>ZEMIN YAO</u>	UNIVERSITY OF OTTAWA HEART INSTITUTE	Attendee	Registered
<u>CHI-LIANG E YEN</u>	UNIVERSITY OF NORTH CAROLINA, CHAPEL HILL	Poster Presenter	Registered
<u>MEI ZHANG</u>	UNIVERSITY OF TEXAS	Attendee	Registered

